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10/693,377	10/24/2003	James Hunter Boone	TLAB.100292	1630

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SHOOK, HARDY & BACON LLP
INTELLECTUAL PROPERTY DEPARTMENT
2555 GRAND BLVD
KANSAS CITY, MO 64108-2613

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	**PAPER NUMBER**
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05/21/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,377	BOONE ET AL.	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/15/2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6-12,15-17,20,24 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-12,15-17,20,24 and 27* is/are rejected.

7)☒ Claim(s) *6 and 7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amended claims 1-2, 6-12, 15-17, 20, 24 and 27 are pending.

Objections/Rejections Withdrawn

1. ***Rejection Withdrawn*** , Claim 8 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is traversed on the grounds that the claim as amended is clear; the claim no longer recites the phrase "for capturing fragments".
2. ***Rejection Withdrawn,*** The rejection of claims 1, 3, 8-11, and 15 under 35 U.S.C. 102(b) as being anticipated by Guerrant et al (US Pat. 5,124,252) is herein withdrawn in light of the amendment of claim 1 to require more than just an obtaining and a single lactoferrin measuring step.
3. ***Rejection Withdrawn*** The rejection of claims 1, 3, and 11 under 35 U.S.C. 102(b) as being anticipated by Fine et al (AJG, 1998)) is herein withdrawn in light of the amendment of claim 1 to require more than just an obtaining and a single lactoferrin measuring step.
4. ***Rejection Withdrawn*** Claims 1, 3 rejected under 35 U.S.C. 102(e) as being anticipated by Moore et al (US Pat. 6,727,073, effective filing date November 19, 1999) is herein withdrawn in light of the amendment of claim 1 to require more than just an obtaining and a single lactoferrin measuring step.
5. ***Claim Objections*** Claims 1 and 12 objected to because of informalities have been amended to obviate the rejection of record. Claim 1 recites the phrase "measuring the sample contains for"; a transitional phrase appears to be missing. Claim 12 recites the phrase "bind to captured lactoferrin" and refers back to the phrase "to create a treated sample"; the term "captured" would only be applicable to a lactoferrin positive sample, the sample of claims 1, 11 and 12 need not be positive for lactoferrin. The samples of claim 1 and 11 from which claim 12 depends, have not been defined to comprise endogenous lactoferrin. Clarification of the sample type (positive for lactoferrin) is requested.

Allowable Subject Matter

6. Claims 11-12, 17 and 20 define over the prior art of record but are rejected under obviousness type double patenting. Obviating the prior art rejection of record over the other claims could obviate the provisional obviousness type double patenting rejection over these claim, resulting in allowable subject matter.

Rejections Maintained/Response to Arguments

7. Applicant's arguments filed January 15, 2009 have been fully considered but they are not persuasive.

8. ***Maintained, Claim Objections*** Claims 6-7 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The combination of claim limitations recited in claims 6 and 7 have been added to claim 1 by amendment; claims 6 and 7 are no longer further limiting of claim 1 from which they indirectly depend.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. The rejection of claim 24, 27 provisionally on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of copending Application No.

2004/0033537 (10/629,975) is traversed by Applicant that the grounds of rejection be held in abeyance until allowable subject matter is indicated.

11. The examiner is maintaining the rejection for reasons of record.

12. The rejection of claim 24 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 7,192,724) is traversed by Applicant that the grounds of rejection be held in abeyance until allowable subject matter is indicated.

13. The examiner is maintaining the rejection for reasons of record.

14. The rejection of claims 1-2, 3, 6-12, 15-17,20 provisionally on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 7-14 of copending Application No. PG-pub 2004,0126898 (10/656,034)) is traversed by Applicant that the grounds of rejection be held in abeyance until allowable subject matter is indicated.

15. The examiner is maintaining the rejection for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending species anticipates the instantly claimed genus of methods, wherein the instant claims do not require the measurement of specific type of immunoglobulin antibodies as claimed in copending claim 13 that measures IgG, IgE, IgM, IgD, IgAsec, IgA and lactoferrin is disclosed to be elevated in subject with disease activity: **[0018] There were 51 ulcerative colitis (UC) patients, 47 Crohn's** disease (CD) patients, 7 irritable bowel patients (IBS), and 11 healthy (H) adults recruited for the study. Fecal specimens were collected from each enrolled patient and stored at -70.degree. C. until tested. Specimen consistency ranged from solid to liquid. The level of fecal ANCA was determined using the qualitative ANCA ELISA as previously described. Disease activity was defined using **elevated fecal lactoferrin** as an indicator of intestinal inflammation. A dilution of 1:10 was used in the qualitative ELISA test and results were reported as positive (absorbance values >0.140) or negative (absorbance values <0.140). The mean optical densities, standard deviation and P values (two-tailed student T-test `with unequal variance) were determined for the ANCA positive ulcerative colitis patients. Of the 26 patients that tested positive for fecal ANCA, there were four patients had Crohn's Disease, 21 had ulcerative colitis and one patient was healthy. ANCA-positive ulcerative colitis showed a mean.+-.SD OD.sub.450 of 0.311.+-.0.166. The mean optical density for the ulcerative colitis patients was significantly different from IBS and healthy persons (p value<0.0005). A summary of the statistical analysis is listed in Table 2.This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

16. ***Maintained, Claim Rejections - 35 USC § 102*** The rejection of claim 24 under 35 U.S.C. 102(b) as being anticipated by Guerrant et al (US Pat. 5,124,252) is traversed on the grounds that:

a. That Guerrant et al does not determine the presence of ASCA and ANCA and

b. determines whether lactoferrin is present in the sample.

17. It is the position of the examiner that Guerrant measured the presence or absence of lactoferrin in a fecal sample, relative to control samples that were all negative on 7 different occasions (see quoted section Guerrant et al, col. 4, lines 12-22, specifically lines 20-22

sion was stored at 4.C until used. Studies with titrations or purified lactoferrin revealed readily apparent agglutination of these latex beads with 0.004–0.0016 mg/ml lactoferrin, at least one log more sensitive than the radial immunodiffusion (RID) assay mentioned above. This level of greater sensitivity of latex agglutination was also seen with ficol-hypaque separated human PMN's as well with a 1:100 dilution being positive when RID detected only a 1:8 dilution. In addition, leukocytes added to stools as well as the *Salmonella* and 4 *C. difficile* cases were positive in the latex agglutination assay. Furthermore, three additional control specimens tested on 7 different occasions were all negative. Importantly, these immunoassay results remained clearly positive even after *C. difficile* cytotoxin totally destroyed the PMN morphology over 24 hours in refrigerated specimens.

18. Additionally, Guerrant et al claims a method of differentiating inflammatory diarrhea from noninflammatory diarrhea, diarrhea being a common symptom held in common between

inflammatory bowel disease and irritable bowel syndrome (see Guerrant et al, claim 1). Nine of 12 samples from children with diarrhea were measured and found to have of lactoferrin that were not elevated, specifically titers of less than 1:50 (see quoted section below). No additional methods steps of selecting and measuring were/are required to diagnosis irritable bowel syndrome (instant claim 3), the 9 samples from children without elevated levels of lactoferrin anticipate the claimed invention set forth in claims 1 and 3 which is associated with a non-inflammatory process arising from the upper small bowel (see Guerrant et al, col. 1, lines 21-22 and claim 1), and unelevated levels of lactoferrin, which is claimed to be diagnostic of IBS.

Further data from children with diarrhea in the northeast of Brazil have shown that specimens from 16 of 17 children with 114 5 or more fecal leukocytes per high power field on microscopy with methylene blue stain had lactoferrin latex agglutination titers of ≥1:50. In contrast, only 3 of 12 methylene blue stained specimens with less than 1 leukocyte per high power field had lactoferrin titers of ≥1:50. Furthermore, despite occasional positives at lower titers, none of 7 specimens from normal control children had lactoferrin titers of ≥1:50.

Both quantitative and qualitative methods are described based upon relative titer (above) and specific ELISA sensitivity values (below, Guerrant et al, col. 4, lines 50-53)

The apparent sensitivity was 0.001 ug/ul or less lactoferrin, with conjugate dilution of 1000 and primary rabbit antibody dilutions of 1:250, probably representing the optimal conditions for assay. The ELISA technology could also be employed in detection of leukocytes, possibly using a dipstick technology.

19. Claim 24 while amended, only carries out the determining steps for ASCA and ANCA when the lactoferrin determination is POSITIVE and ELEVATED. Guerrant et al was applied against the claims for when the patient sample is negative or lactoferrin is present with

unelevated lactoferrin levels. When the samples are negative, the additional tests are not required by the claims. With respect to claim 24, when the lactoferrin level is not elevated, Guerrant et al determines that the patient has non-inflammatory diarrhea, a symptom of irritable bowel syndrome. While Guerrant et al (see preamble of allowed claims) does not refer to non-inflammatory diarrhea as irritable bowel syndrome, a patient that presents with diarrhea and does not have elevated levels of lactoferrin, would not have inflammatory bowel disease, and would be a patient with irritable bowel. Therefore Guerrant et al still anticipates the instantly claimed invention as now claimed, for reasons of record and responses set forth herein.

20. Claim 24 is rejected under 35 U.S.C. 102(b) as being anticipated by Guerrant et al (US Pat. 5,124,252).
Instant claim 24: Guerrant et al disclose the instantly claimed invention directed to a method, the method comprising the steps of:
21. obtaining a fecal sample from a person (see abstract);
22. determining whether lactoferrin is present in the sample (three additional control specimens tested on 7 different occasions were all negative (see col. 3, lines 63-64) and 9 of 12 samples did not evidence elevated levels of lactoferrin, the samples obtained from children with diarrhea.
Instant claim 8-10: wherein the presence of lactoferrin is measured by ELISA (see col. 4, lines 23-60, especially lines 30-31).
Instant claim 11:further comprising diluting the sample (see col. 2, lines 38-42 "mixed with an equal amount of 0.1% Triton-X".)
Instant claim 12: further comprising contacting the sample with immobilized polyclonal antibodies "Bacto-latex beads were coated with rabbit anti-human lactoferrin" and this latex bead suspension was added to "22 fecal specimens (see col. 4, lines 1-11), the endogenous lactoferrin being released by the leukocytes (see col. 4, lines 12-16 "children with diarrhea in the northeast of Brazil"). further comprising contacting said treated sample with enzyme liked polyclonal antibodies to create a readable sample (see col. 4, lines 42-44 "peroxidase conjugation", read both visually and spectrophotometically (see col. 4, line 49 and claim 4). While the reference is silent with respect to whether the rabbit antibodies are polyclonal or monoclonal antibodies, it is clear that the reference does not discuss nor describe the production of hybridoma and monoclonal production, therefore the antibodies are conventional rabbit sera that comprise polyclonal antibodies.
Instant claim 15: further comprising generating a purified lactoferrin standard curve (see col. 4, lines 29-32, varying concentrations of lactoferrin were coated in the wells). The sensitivity of the assay was 0.001 ug/ml or less lactoferrin (see claim 4). Guerrant et al (US Pat. 5,124,252) anticipates the instantly claimed invention that does not require the claimed method to measure anything more than endogenous lactoferrin when the sample when the lactoferrin determination is considered negative in light of all the claims reciting the phrase "if so", which makes the following methods steps optional. Guerrant et al (US Pat. 5,124,252) anticipates the instantly claimed invention as now claimed.

23. The rejection of claims 24 and 27 under 35 U.S.C. 102(b) as being anticipated by Fine et al (AJG, 1998) is asserted to require the determining whether or not the fecal sample has an elevated level of ASCA or ANCA.

24. It is the position of the examiner that the method of claim 24 does not require the determining of ASCA or ANCA when the sample is negative or does not evidence an elevated level of lactoferrin in the fecal sample; this embodiment is disclosed in Fine et al. The rejection is maintained for reasons of record and responses set forth herein.

Instant claim 1, 3 and 24, 27: Fine et al disclose the instantly claimed invention directed to a method, the method comprising the steps of:

25. obtaining a fecal sample from a person (see page 1301, col. 2, first two paragraphs);

26. determining whether lactoferrin is present in the sample (see page 1302, Table 1 "Diagnoses in 92 Patients with a negative fecal lactoferrin Test",

Instant claim 27: one patient's test changed levels upon repeating the lactoferrin determination (see page 1302, Table 1, bottom of ledger narrative). The lactoferrin data was used to distinguish the patients that have inflammatory bowl disease or syndrome from those patients that have another bowl condition (see page 1302, Table 1).

Instant claim 11: further comprising diluting the sample (see page 1301, col. 2, paragraph 3); further comprising contacting the sample with immobilized polyclonal antibodies latex beads were coated with rabbit anti-human lactoferrin, the endogenous lactoferrin is detected with the immobilized polyclonal antibodies. While the reference is silent with respect to whether the rabbit antibodies are polyclonal or monoclonal antibodies, it is clear that the reference does not discuss nor describe the production of hybridoma cell lines and monoclonal antibody production, therefore the antibodies are present in conventional rabbit sera that comprise polyclonal antibodies.

Fine et al anticipates the instantly claimed invention that does not require the claimed method to measure anything more than endogenous lactoferrin when the lactoferrin determination is considered not elevated in light of claim 3 being directed to diagnosis of IBS which does not require the additional selecting and measuring steps of claim 1 or claim 24, which makes the following methods steps optional. Fine et al still anticipates the instantly claimed invention as now claimed.

27. ***Maintained, Claim Rejections - 35 USC § 103 The rejection of c***laims 1-3,6-10, 24 and 27 under 35 U.S.C. 103(a) as being unpatentable over Nielsen et al (2000) in view of Targan et al (1995) and Fine (PG-Pub 2001/0036639A1, filing date March 2, 2001) is traversed on the grounds that:

c. Nielsen et al disclose testing for ASCA and ANCA in a serum sample,

d. the sample of Targen is a serum sample and

e. Fine does not teach elevated levels of ANCA or ASCA in a fecal sample.

28. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

1. It is the position of the examiner that Nielsen et al teach Lactoferrin to be a fecal marker for inflammatory bowel disease (see page 360, col. 2, lines 3-5) and the importance of measuring ASCA and ANCA for distinguishing UC from Crohn's disease.

2. Nielsen et al additionally teaches the importance of distinguishing between inflammatory bowel disease patients, specifically distinguishing between ulcerative colitis (UC) and Crohn's disease (CD)(see page 359, col. 2, middle of second paragraph). Nielsen et al goes on to teach that pANCA is more common in UC than CD (see page 361, col. 2, paragraph 1) and that ASCA, antibodies to Saccharomyces cerevisiae, also known as bakers yeast, is a marker for Crohn's disease (see page 361, col. 2, paragraph 2). Nielsen et al teaches the combined measurement (see page 361, col. 2, p. 3) of both ANCA and ASCA in order to gain insight into sub classification of inflammatory bowel disease patients. Therefore, Nielsen et al clearly teaches measuring all three markers for assessment of disease activity in inflammatory bowel disease patients. The examiner agrees Nielsen et al is not applicable to the claims under 35 USC 102, but was applied against the claims under 35 USC 103, in view of guidance and teaching provided by Targan and Fine.

3. Applicant states that Targan et al analyze serum samples and do not teach elevated levels of ANCA in a fecal sample.

4. It is the position of the examiner that ANCA autoimmune antibodies are not normal antibodies that would not be present in a normal subject sample, and present in a subject with a disease condition. Detectable levels of ANCA would be elevated over normal which would be undetectable in a normal sample.

It is also the position of the examiner that Targan et al clearly teach the intestinal B cells to be the source of serum antibodies, the intestinal B cells expressing pANCA are associated with fecal material into which they would express pANCA antibodies. The person of ordinary skill in the art would have been motivated and would have a reasonable expectation of success of measuring pANCA antibodies in a fecal sample from a patient with UC as Targan et al teach 70% of UC patient produce pANCA antibodies from B cells from an intestinal sample.

5. Targan et al states ANCA is found in serum of ulcerative colitis patients, and focuses on measuring ANCA antibodies produced by B-cells in the colonic mucosa (see page 3262, col. 2, last sentence). The purpose of Targan et al's study is defined in col. 1, paragraph 1, on page 3263 where Targan et al found pANCA expressing cells in the mucosa of intestinal tissue (see patient population, sample were obtained from intestinal tissue, page 3263, col. 1, paragraph 2).

Figure 1 and Table 1 on page 3264 show patients with diverticulitis (non-IBD) and Crohn's disease to not significantly produce ANCA antibodies, while ANCA antibodies are significantly produced in UC patients . On page 3265, Discussion section, Targan et al state that "This study demonstrate the presence of ANCA-secreting B-cells within the mucosal LPL fraction from 70% of patients with UC." Targan et al site two additional studies that support

their finding that "the intestinal mucosa may be a unique source of autoantibody producing B-cells". One of these results "indicates that B cells may be directly activated in the mucosal compartment by enteric Ags, and suggests that the presence of Ab in serum is due to spill over of that production. Therefore, antibodies in fecal samples would not only come from the serum, but from B cells producing antibodies in the mucosal compartment of the intestine (see page 3265, col. 2, middle and end of first paragraph). Targan et al in summarizing their work states that their study indicated that "pANCA are being produced by local B cell populations within the lamina propria and are limited to mucosal tissues from UC patients", as well as states "Under appropriate conditions that result in chronic inflammation, such as are found in ileal pouches (ie., bacterial overgrowth and/or fecal stasis), these B cells are triggered to express pANCA.(page 3266, col. 2, first paragraph)" .

29. It is the position of the examiner that Fine et al teach the presence of ASCA antibodies can be measured/determined in fecal samples. With respect to differential diagnosis of irritable bowel syndrome and inflammatory bowel disease, Fine et al teaches the essential criteria for differentiating these two conditions. Additionally, Fine et al still teaches the detection, measurement of ASCA antibodies from bakers' yeast which is also taught by Nielsen et al to be the source of these auto antibodies, the yeast being Saccharomyces cerevisiae (see Nielsen page 381, col. 2,p. 2). Clearly Nielsen et al and Fine et al are analogous art.

30. Nielson et al describe biological activity markers of Inflammatory Bowel Disease (see title, page 359), wherein the markers include fecal lactoferrin (see page 360, col. 2, paragraph 1),

and auto antibodies known as ANCA and ASCA (see page 361, col. 1-2). Nielson et al teach the methods step of :

Obtaining a fecal sample from a patient and determining the presence of fecal lactoferrin (see page 360, col. 2, paragraph 1) in order to provide for both sensitive and bowel-specific markers of disease, and further determining the presence or absence of ASCA and ANCA in the patient (see page 361, col. 1-2).

Nielson et al teach the importance of assessing disease activity in inflammatory bowel disease (IBD), to include ulcerative colitis and Crohn's disease based upon clinical parameters and various biological disease markers (see page 359, col. 1, abstract, first sentence), but differs from the instantly claimed invention by failing to determine ANCA and ASCA in the fecal sample.

Targan et al (1995) teach ANCA antibodies are present in mucosal lesions of the bowel (whole abstract; and page 3266, col. 2, paragraph 1) in ulcerative colitis patients (non-serum samples, see table II, page 3265; p3264, Figure 1, Table 1; diluted 1:2 (see page 3264, Results section, first paragraph) in an analogous art for the purpose of quantitatively (see Table 1, page 3264, col. 5) defining pANCA production is a consequence of a mucosal immune response associated with ulcerative colitis (full last sentence of abstract; Fig. 1, p 3264).

Fine et al (20010036639) teach a method of measuring fecal antibodies directed to Saccharomyces pervasive (ASCA) (see claims 1, 19-21 and 43; [0054]) in an analogous art for the purpose of determining the presence of antibodies associated with diseases or disorders of the bowel, to include diagnosis of irritable bowel syndrome (see page 3, [0020] and [0015; 0018, entire paragraph, as well as second half of paragraph. "diarrhea"]).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to measure fecal lactoferrin, ANCA and ASCA in a patient fecal sample because Nielson et al teach biological markers associated with inflammatory bowel disease, and teach fecal lactoferrin, as well as ANCA and ASCA to provide insight into disease activity associated with inflammatory bowel disease (see Nielsen et al, abstract, page 360, col. 2, p.1 and page 361, col. 1-2) and Targan et al and Fine et al teach the presence of ANCA and ASCA markers, respectively, are present in fecal/mucosal bowel samples and could be measured in the patient fecal sample along with the fecal lactoferrin determination. The person of ordinary skill in the art would have been motivated to determine fecal lactoferrin, along with fecal ANCA and ASCA markers because Nielsen et al teach that the lactoferrin is a measure of active bowel disease and measurement of ANCA and ASCA provide for differential diagnosis of the patient's type of inflammatory bowel disease (see Nielsen et al, page 361, col. 2, paragraph 3).

In the absence of a showing of unexpected results, the person of ordinary skill in the art would have been motivated by the reasonable expectation of success of determining the presence or absence of inflammatory bowel disease (see page 360, col. 1, p. 1) by determining the fecal lactoferrin test, a marker for active bowel inflammatory disease, as taught by Nielsen et al, and if positive, further determining the presence and amount of ANCA and ASCA antibodies in the fecal sample because Nielsen et al teach that the "combined measurement of pANCA and ASCA may be used advantageously in the sub-classification of IBD patients with indeterminate colitis. Both antibody specificities are measured by traditional quantitative solid phase immunosorbent assays, and they are highly specific (>90%) for both UC and CD with disease sensitivity around

50% in both cases (see Nielsen et al, page 361, col. 2, paragraph 3)." Nielsen et al in view of Targen et al and Fine et al obviate the instantly claimed invention as now claimed.

Conclusion

31. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

32. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ginny Portner/
Examiner, Art Unit 1645
May 8, 2009

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645